Remarks

The Office Action mailed October 13, 1006 has been received and reviewed. Claims 27, 28, and 48-52 having been amended, the pending claims are claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27, 28, and 43-66. Claims 60-66 being withdrawn from examination, as drawn to non-elected inventions, the claims currently under examination are 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27, 28, and 43-59. Reconsideration and withdrawal of the rejections are respectfully requested.

Support for the recitation "fluorochrome" in amended claims 27, 28, and 48-52 is found, for example, on page 13, line 16 and page 36, line 7 of the specification. Support for the recitation "in culture" in amended claims 27 and 48-52 is found, for example, in original claim 28 and on page 39, lines 28-33 of the specification. Applicant submits that no new matter and no new issues for examination are raised by these amendments.

35 U.S.C. §103/35 U.S.C. §112, first paragraph, "Squeeze"

Under 35 U.S.C. §103, "[t]he prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (see MPEP § 2143.02). Likewise, "[a]ny analysis [under 35 U.S.C. §112, first paragraph,] of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention," and "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation" (see MPEP 2164.01). "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (see MPEP 2164.03).

Applicant respectfully submits that the Patent Office must apply a consistent standard when analyzing and rejecting claims under 35 U.S.C. §103 and 35 U.S.C. §112, first

paragraph. Applicant submit that the Examiner has not done so in the instant case, rejecting the claimed methods as *prima facie* obvious over the prior art, asserting that there is a reasonable expectation of success with combining prior art teachings to obtain the claimed methods, yet rejecting the same claims as not enabled by the teachings of the specification combined with other knowledge available to the skilled artisan. Applicant submits that this is improper. Reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. §103 and 35 U.S.C. §112, first paragraph, is requested.

The 35 U.S.C. §103 Rejection

The Examiner rejected claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28, and 43-59 under 35 U.S.C. §103(a) as being unpatentable over WO 99/61040 (the '040 publication) or U.S. Patent No. 6,492,325 (the '325 patent) in view of Nykvist et al. (JBC 275(11):8255-8261, 2000), U.S. Patent No. 5,567,440 (the '440 patent) and Lin et al. (Development 128, 1573-1585 (2001)). This rejection is traversed. In rejecting claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28, and 43-59 under 35 U.S.C. §103(a) (see paragraphs 12 and 13, pages 6-9 of the Office Action mailed October 13, 2006), the Examiner made the following assertions:

-The '040 publication and the '325 patent teach methods of treating chronic inflammatory diseases of the kidney by administering an effective amount of an α1β1 integrin receptor inhibitor, wherein the agent is an antibody;

-The claimed invention differs from the '040 publication or the '325 patent only by the recitation of an antibody to Collagen XIII;

-Nykvist et al. teach that α1β1 integrin mediates cell adhesion to type XIII Collagen;

-The '440 patent teaches that cell adhesion plays an important role in human disease. These interactions proceed by the interaction of receptors upon the surface of a cell with proteins . . . upon the surface of another cell or within the extracellular matrix. The '440 patent further teaches that routes to the interruption of these interactions typically involve competitive inhibition of these receptor-ligand interactions, for example, with antibodies;

-Lin et al. teach two collagen XIII blocking antibodies, ELQ and Q36.4;

-Given that Nykvist et al. teach "that α1β1 integrin mediates cell adhesion to type XIII collagen," and "given the fact that routes to the interruption of cell adhesion interactions typically involve competitive inhibition of these receptor-ligand interactions with . . .[, for example,] antibodies, it would have been obvious to one of ordinary skill in the art . . . to substitute the α1β1 integrin receptor inhibitor such as an antibody as taught by the '040 publication or the '325 patent with the anti-collagen type XIII antibody taught by Lin et al.";

-"Further, a person of ordinary skill would have recognized the inter-changeablility of the element shown in the prior art for the corresponding anti-collagen type XIII blocking antibodies"; and

-"From the combined teachings of the references, ***it is apparent that one of ordinary skill in the art would have a reasonable expectation of success in producing the claimed invention"*** (emphasis added).

-Therefore, the invention as a whole is *prima facie* obvious.

While Applicant respectfully disagrees, Applicant takes notice of both the level of ordinary skill in the art and the level of predictability in the art established by the Examiner in making this rejection. In view of these assertions, withdrawal of the rejection of the claims as not enabled under 35 U.S.C. §112, first paragraph, is requested.

To substantiate this rejection, the Examiner relies on the teachings of Lin et al., asserting that Lin et al. "teaches two ***collagen type XIII*** blocking antibodies ELQ and Q36.4" and that "it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the α1β1 integrin receptor inhibitor such as an antibody taught by the '573 application with ***anti-collagen XIII*** antibody taught by Lin et al." (see, for example, page 7 of the Office Action mailed October 13, 2006 (emphasis added)). Applicant submits that the Examiner's interpretation of the teachings of Lin et al. is incorrect. Lin et al. does not teach antibodies to ***collagen XIII*** (that is, collagen "13"), rather, Lin et al. teach antibodies to ***collagen XVIII*** (that is, collagen "18"). To establish a *prima facie* case of obviousness, "the prior art reference (or references when combined) must teach or suggest all the claim limitations" (MPEP §§ 706.02(j) and 2143.03)). Lin et al. provide no teachings of antibodies to Collagen XIII. Applicant respectfully submits that claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28, and 43-59

are not obvious over WO 99/61040 or U.S. Patent No. 6,492,325 in view of Nykvist et al., U.S. Patent No. 5,567,440, and Lin et al. Reconsideration and withdrawal of this rejection of the claims under 35 U.S.C. §103 is requested.

The 35 U.S.C. §112, First Paragraph, Enablement Rejection

The Examiner rejected claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28 and 43-59 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is traversed.

Specifically, the Examiner asserted that "the specification fails to provide empirical data to show that [the] method would work in vivo" (page 4, Office Action mailed October 13, 2006). Applicant submits that "[c]ompliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed" (MPEP 2164.02).

Further, the Examiner asserted that "[t]he state of the art is that current treatments of inflammation/conditions associated with the interaction of Collagen XIII with α1β1-integrin positive monocytes, is in fact unknown and untested" (page 5, Office Action mailed October 13, 2006). Further, the Examiner asserted that "there is no correlation on this record between in vitro experiments and a practical method of in vivo use in currently available form for humans or animals" (page 5, Office Action mailed October 13, 2006). Applicant remind the Examiner of earlier assertions (in the rejection of the same claims as obvious under 35 U.S.C. §103), that one of ordinary skill in the art would have a reasonable expectation of success in practicing the claimed invention. Applicant submits that the specification provides adequate enablement for the claimed methods.

Finally, the Examiner asserted that "the skilled medical practitioner would not be able to identify all chronic inflammatory diseases or conditions associated with the interaction of Collagen XIII with α1β1 integrin monocytes based on the disclosure" (page 5, Office Action mailed October 13, 2006). First, Applicant does not understand the relevance of this assertion to the methods of claims 7, 8, 10-13, 15, 17, 21, 23, 25, 28, 43-47, and 49-59. Further, Applicant

submits that chronic inflammatory diseases or conditions are well known and identifiable by the skilled practitioner.

In view of the above discussion, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §112, first paragraph, as not enabled by the specification, is requested.

The 35 U.S.C. §112, First Paragraph, New Matter Rejection

The Examiner rejected claims 1-3, 5-6, 27 and 53 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. This rejection is traversed.

The Examiner asserted that the recitation "a progressive renal fibrosis, the method comprising administering to the patient an antibody to collagen XIII" in claim 43 is not supported by the specification. No such recitation is found in claim 43. Clarification is requested

The Examiner asserted that the recitation "a chronic inflammatory disease associated with the interaction of collagen XIII with α1β1 positive monocytes" in claim 1 is not disclosed in the specification and claims, as originally filed. Applicant disagrees and submits that the specification and claims, as originally filed, provide ample support for claim 1. Applicant directs the Examiner to original claims 1 and 6, drawn to "[a] method of treating a patient having a chronic inflammatory disease, the method comprising administering to the patient a blocking agent to neutralize the capacity of Collagen XIII to bind to a α1β1 integrin" (claim 1) and "[t]he method of claim 1 wherein the blocking agent blocks the interaction of α1β1 integrin on peripheral blood monocytes and/or lymphocytes with Collagen XIII" (claim 6). Applicant submits that claims 1 and 6, as originally filed, provide support for the recitation "a chronic inflammatory disease associated with the interaction of collagen XIII with α1β1 positive monocytes." Further, Applicant directs the Examiner to the following portions of the

specification, for additional support. "In another embodiment, the present invention provides a method for treating a subject having an inflammatory disease . . . where integrin α1β1-positive interstitial monocyte and/or lymphocyte accumulation is observed. The method involves administering . . . an active agent that disrupts the interaction between Collagen XIII and α1β1 integrin. Preferably, the active agent blocks binding of Collagen XIII . . . (on vascular endothelium of chronically inflamed tissues) and α1β1 integrin" (see page 2, lines 26-32). And, "[b]locking the ability of Collagen XIII to bind to α1β1 integrin will be therapeutically beneficial for any chronic inflammatory disease where integrin α1β1-positive interstitial monocyte accumulation is observed" (page 12, lines 16-19 of the specification).

Further, the Examiner asserted that the specification does not provide support for the use of an anti-Collage XIII antibody in the method of claim 43. Applicant disagrees and directs the Examiner to original claims 7 and 11 (drawn to methods "for treating a subject having an inflammatory disease or other condition where integrin α1β1-positive interstitial monocyte and/or lymphocyte accumulation is observed, the method comprising administering to the subject an active agent that disrupts the interaction between Collagen XIII and α1β1 integrin" (claim 7); "wherein the inflammatory disease or other condition is renal fibrosis (claim 11)) and to page 11, lines 19-30 of the specification ("the present invention provides a method of reducing the rate of monocyte . . . efflux into the interstitial space of chronically inflamed tissues. This method involves . . . contacting the α1β1 integrin on the cell surface of lymphocytes . . . with an agent that disrupts . . . the interaction between Collagen XIII and α1β1 integrin. This can result from the use of an active agent such as a peptide fragment of Collagen XIII . . . . Alternatively, this method can involve the use of an active agent, such as a mono-specific ***antibody***, that binds Collagen XIII" (emphasis added)). Applicant respectfully submit that the specification contemplates using an antibody to Collage XIII in the method of claim 43.

In view of the above discussion, reconsideration and withdrawal of the rejection of claims 1-3, 5-6, 27 and 53 under 35 U.S.C. §112, first paragraph, as containing new matter, is requested.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claims 27-28 and 48-52 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is traversed.

Specifically, the Examiner asserted that the recitation "Alexa" in claims 27, 28, and 48-52 is indefinite. Applicant submits that this rejection is overcome in view of the amendment of claims 27, 28, and 48-52 to recite "fluorochrome."

Further, the Examiner asserted that Claims 27-28 and 48-52 "are indefinite because it is unclear how the referenced antibodies would inhibit binding of Alexa-conjugated purified α1β1 integrin to MCP-1 treated primary endothelial cells in vivo" (page 2, Office Action mailed October 13, 2006). Claim 28 recites "wherein the antibody inhibits the binding of fluorochrome-conjugated purified α1β1 integrin to MCP-1-treated vascular endothelial cells ***in culture***" (emphasis added). Applicant respectfully submits that this recitation is describing a functional characteristic of the antibody, that the antibody inhibits binding ***in culture***, that is in vitro. Applicant submits that the metes and bound of claim 28 are clear. Likewise, claims 27 and 48-52, as amended, also recite "in culture." Applicant submits that the metes and bounds of claims 27 and 48-52 are also clear.

In view of the above discussion, reconsideration and withdrawal of the rejection of claim 27, 28, and 48-52 under 35 U.S.C. §112, second paragraph, is requested.

Double Patenting Rejection

Claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28, and 43-59 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25, 34-36, 40, 43-45, and 52 of copending Application No. 10/099,573 (the '573 application) in view of Nykvist et al., U.S. Patent No. 5,567,440 and Lin et al. This rejection is traversed. To substantiate this rejection, the Examiner relies on the teachings of Lin et al., asserting that Lin et al. "teaches two ***collagen type XIII*** blocking antibodies ELQ and Q36.4" and that "it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the α1β1 integrin receptor inhibitor such as an antibody taught by the '573

application with ***anti-collagen XIII*** antibody taught by Lin et al." (Pages 10 and 11, Office Action mailed October 13, 2006 (emphasis added)). Applicant submits that the Examiner's interpretation of the teachings of Lin et al. is incorrect. Lin et al. does not teach antibodies to ***collagen XIII*** (that is, collagen "13"), rather, Lin et al. teach antibodies to ***collagen XVIII*** (that is, collagen "18"). Lin et al. provide no teachings of antibodies to Collagen XIII. Withdrawal of this provisional rejection of claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28, and 43-59 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25, 34-36, 40, 43-45, and 52 of copending Application No. 10/099,573 in view of Nykvist et al., U.S. Patent No. 5,567,440 and Lin et al. is requested.

Summary

It is respectfully submitted that the pending claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27, 28, and 43-66 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicant's Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
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